In utero irradiation-induced alterations in the mouse brain characterised by 3D T_2-weighted MRI

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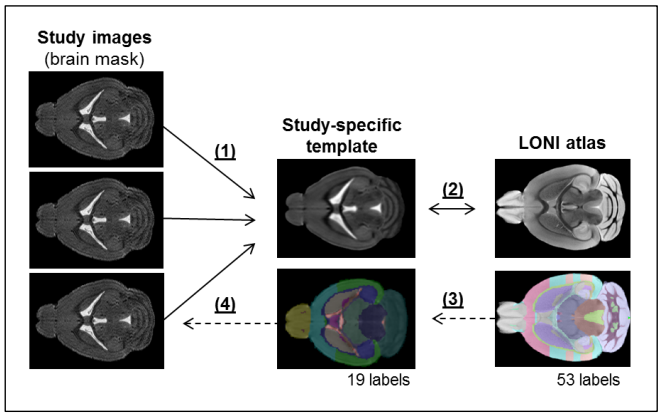
Introduction: Ionising radiation exposure during pregnancy is known to cause a higher incidence of neurological defects such as mental retardation and small brain size (microcephaly). Epidemiological studies have indicated that such deficits can occur after exposure to low doses (≤ 0.10 Gy). However, animal studies are scarce and underpinning mechanisms remain unclear. In this study, we quantified the cross-sectional *in vivo* morphological differences among irradiated mouse brains using atlas-based segmentation of 3D T_2-weighted MR images.



Methods: At E11, pregnant mice were X-irradiated with different doses (0.00, 0.10, 0.33, 0.66 and 1.00 Gy). The female offspring was imaged at 22 weeks of age. For morphological characterisation of the brain images, a semi-automatic small animal image analysis pipeline, which sequentially corrects for radiofrequency inhomogeneity, pose and inter-scan variation, was used (Rangarajan et al. 2011). Consequently, all study images were automatically registered (Maes et. al. 1997) to a reference, i.e. a representative control image that was spatially normalised to the LONI atlas (MacKenzie-Graham et al. 2004). The brain mask of this reference image was then propagated to each of the study images. The corresponding skull-stripped brain images of control animals were iteratively co-registered to construct a study-specific mean deformation template by non-rigid registration (Rueckert et al. 1999, Modat et al. 2010) **(1)**. Next, by automatically co-registering this template to the LONI atlas **(2)**, a pilot segmentation of 19 brain structures was obtained **(3)**. After manual correction, these anatomical labels were propagated to the individual study images using the transformations determined in the template construction step **(4)**. Regional brain volume changes across different experimental conditions were quantified and compared with the controls.

Results: The brain volume of prenatally irradiated mice (0.33, 0.66 and 1.00 Gy) decreased significantly when compared to controls. As such, all brain structures were reduced in volume as well. However, preliminary data point towards an additional reduction of the volume of the cerebral cortex and hippocampus. Notably, these brain structures are linked to performance in the Morris water maze, which was indeed defected in these irradiated animals.

Conclusions: The atlas-based segmentation approach clearly revealed a reduction in brain size/volume in high-dose exposed mice while the brain size of low-dose irradiated animals was not different from controls. However, registration results can additionally be used for voxel-wise comparison of brain images, which might demonstrate more subtle differences.

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Abstract category:

- ☐ Cancer
- ☒ Neurology
- ☐ Novel technologies, methodologies and modalities
- ☐ Other